UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/344,676	06/25/1999	WILLIAM P. VAN ANTWERP	PD-0310	9328

22462 7590 06/28/2004

GATES & COOPER LLP
HOWARD HUGHES CENTER
6701 CENTER DRIVE WEST, SUITE 1050
LOS ANGELES, CA 90045

EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 06/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/344,676	VAN ANTWERP ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,8,9,11,17,19-21,59,61,62,64-66 and 71* is/are pending in the application.

4a) Of the above claim(s) *1,5,8,9,11,17,19,20,59,61,62,64-66 and 71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the directives of the amendment filed 6/15/04, claims 1, 59 and 61 have been amended. Claims 1-3, 5, 8, 9, 11, 17, 19-21, 59, 61, 62, 64-66, 71 are now pending. Claims 1, 5, 8, 9, 11, 17, 19, 20, 59, 61, 62, 64, 65, 66, 71 remain withdrawn from consideration.

Claims 2, 3 and 21 are examined in this Office action.

The term "**CMC**" is used hereinbelow as an abbreviation for "critical micellar concentration"

. . . .

Applicants' arguments filed 6/15/04 have been considered and found not persuasive.

The response filed 6/15/04 questions the withdrawal of claim 20 from consideration, arguing that claim 20 had previously been considered to fall within the scope of the elected subject matter. Regardless of whether claim 20 might have previously fallen within the scope of the elected composition, claim 20, according to one interpretation, does not necessarily encompass the elected composition. Claim 20 as previously presented (see, for example the amendment filed 6/25/03) required the presence of insulin *per se*. The claim also permitted an insulin analog to be present, and permitted an "insulin-related peptide" to be present, but claim 20 required that insulin *per se* be present. The amendment filed 12/22/03 eliminated the requirement for insulin (*per se*) from the

composition of claim 1, and by so doing, eliminated the requirement for insulin (*per se*) from claim 20. The elected composition (response, 7/3/02) required the presence of human insulin. Since claim 1 has been amended to exclude the elected composition, withdrawal of claims 1 and 20 from consideration is justified. The response filed 6/15/04 also observes that claim 59 was withdrawn in the Office action mailed 3/18/04, but was not withdrawn prior to that. However, no argument is made as to how or why claim 59 falls within the scope of the elected composition.

The response filed 6/15/04 also argues that "merely adding a further limitation in a dependent claim cannot create a separate invention for restriction purposes". However, this is not necessarily true. To take a very simplistic example, suppose that the following two claims were presented by an applicant, and that the applicant elected an "orange" as the fruit:

1. A basket containing an apple.

2. The basket of claim 1 further containing an orange.

In such a case, claim 1 could be properly withdrawn from consideration, since it does not require the presence of an orange. The response (filed 6/15/04) also offers a quote from the MPEP §806.03, which makes references to a "single disclosed embodiment of an invention". However, it is hardly the case that instant claim 20 (or instant claim 1) is drawn to a "single disclosed embodiment of the invention". Claim 20 is drawn to a very

broad genus, which is potentially of infinite size. Accordingly, it is maintained that claim 20 does not necessarily encompass the elected composition.

✧

Claims 2 and 3 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of claims 2 and 3 is dependent on a non-elected claim.

✧

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 2, 3 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Walter

H. M. (*Diabetes Research* **13** (2) 75-7, 1990) in view of Rieveley (USP 6,153,632).

As indicated previously, Walter discloses (page 76, col 1, paragraph 2) "HOE 21 PH" insulin which is insulin combined with the surface-active stabilizer polyethylene - polypropylene glycol. Also disclosed (page 76, col 1, paragraph 2) is that the genapol was used at a concentration of 10 micrograms per mL. Also disclosed (e.g., page 76 col 2) is that use of the "HOE 21 PH" insulin resulted in less catheter occlusion and a "significant improvement of metabolic control". Walter does not suggest combining insulin with an insulin sensitizer.

As indicated previously, Rieveley discloses (e.g., col 4, line 50+) a composition comprising insulin and an insulin sensitizer. As stated (col 4, line 56+), the effect of the insulin sensitizer is to sensitize the cells of the mammal so as to enhance insulin uptake and/or utilization of glucose by the cells of the mammal thus reducing the therapeutic dose of insulin that is required. Rieveley does not teach combining insulin with the surface-active stabilizer polyethylene - polypropylene glycol.

The response filed 6/15/04 argues that the examiner has not commented on the requirement in the claims for "an insulin analog". The term "insulin analog" would include a peptide which is obtained by adding or deleting a single methylene unit from the side chain of an amino acid. Following are examples of such a substitution: ornithine for lysine, aminopentylglycine for lysine, phenethylglycine for Phe, homocysteine for

cysteine, ethylglycine for alanine, aspartic acid for glutamic acid, or glutamine for asparagine. The peptide chemist of ordinary skill would have expected that substituting **one** of the amino acid side chains with a close homolog thereof will result in a peptide with substantially identical activity [*In re Shetty* (**195** USPQ 753) and *In re Hass & Susie* (**60** USPQ 544)].

The response filed 6/15/04 argues that the examiner has not commented on the requirement in claim 21 for an "insulin-related peptide" which is "coated" with a surfactant. As indicated on page 5, line 1+ (specification), an "insulin-related peptide" is a peptide that exhibits the physiological activity of an insulin related peptide, and which has at least one amino acid different (from the insulin related peptide). Certainly, insulin itself is "related" to insulin; insulin could in fact be viewed as the epitome of an "insulin-related peptide", since it is more like insulin than any other peptide. As above, the requirement for one amino acid difference is met by substituting the side chain of one amino acid with a close homolog thereof. Consider next the limitation of "coating" a "hydrophobic portion" of the insulin-related peptide. It is apparent from the specification that such coating occurs by combining insulin with the genapol surfactant. In addition, in the examples provided (pages 11 and 12), the concentration of genapol used by applicants was identical to that used by Walter. Accordingly, if the "coating" occurs in the examples (specification), it must also occur in the hands of the chemist who has prepared the

composition in accordance with the directives of Walter.

The rejection is maintained.

Claims 2, 3 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Grau (*Diabetes* **36** (12) 1453-1459, 1987) in view of Rieveley (USP 6,153,632).

Grau discloses (page 1453, col 2) "HOE 21 PH" insulin which is insulin combined with the surface-active stabilizer polyethylene - polypropylene glycol. Also disclosed is that the "HOE 21 PH" reduces the precipation and catheter occlusion that would otherwise occur with insulin alone. Also disclosed (page 1453, col 2) is that the surfactant was used at a concentration of 10 micrograms per mL. Grau conveys that "HOE 21 PH" insulin is advantageous when used with insulin infusion pumps. As indicated previously, Rieveley discloses (e.g., col 4, line 50+) a composition comprising insulin and an insulin sensitizer. As stated (col 4, line 56+), the effect of the insulin sensitizer is to sensitize the cells of the mammal so as to enhance insulin uptake and/or utilization of glucose by the cells of the mammal thus reducing the therapeutic dose of insulin that is required.

The response filed 6/15/04 does not traverse this rejection separately from that of the §103 over Walter in view of Rieveley, and so the examiner's arguments with respect thereto are incorporated by reference herein.

The rejection is maintained.

✧

Claims 2, 3 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Walter H. M. (*Diabetes Research* **13** (2) 75-7, 1990) in view of Clark (USP 5,783,556) further in view of Rieveley (USP 6,153,632).

As indicated above, Walter discloses (page 76, col 1, paragraph 2) "HOE 21 PH" insulin which is insulin combined with the surface-active stabilizer polyethylene - polypropylene glycol. Also disclosed (e.g., page 76 col 2) that use of the "HOE 21 PH" insulin resulted in less catheter occlusion and a "significant improvement of metabolic control". Also as indicated previously, Clark discloses a composition comprising insulin and IGF-1. It is disclosed (e.g., col 20, line 52+) that coadministration of insulin and IGF-I leads to unexpectedly lower glucose levels, which is advantageous in the management of diabetic patients. As indicated previously, Rieveley discloses (e.g., col 4, line 50+) a composition comprising insulin and an insulin sensitizer. As stated (col 4, line 56+), the effect of the insulin sensitizer is to sensitize the cells of the mammal so as to enhance insulin uptake and/or utilization of glucose by the cells of the mammal thus reducing the therapeutic dose of insulin that is required.

The response filed 6/15/04 does not traverse this rejection separately from that of the §103 over Walter in view of Rieveley, and so the examiner's arguments with respect thereto are incorporated by reference herein.

The rejection is maintained.

✧

Claims 2, 3 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Walter H. M. (*Diabetes Research* **13** (2) 75-7, 1990) in view of Cooper (USP 5,641,744), further in view of Rieveley (USP 6,153,632).

As indicated above, Walter discloses (page 76, col 1, paragraph 2) "HOE 21 PH" insulin which is insulin combined with the surface-active stabilizer polyethylene - polypropylene glycol. Also disclosed (e.g., page 76 col 2) that use of the "HOE 21 PH" insulin resulted in less catheter occlusion and a "significant improvement of metabolic control". Walter does not suggest combining insulin with an insulin sensitizer or with amylin.

As indicated previously, Cooper discloses (e.g., col 3, line 37+) a composition comprising insulin and amylin. Cooper also discloses (col 3, line 57+) that the combination provides "tighter diabetic control with reduced risk of hypoglycemia". Cooper does not disclose the use of insulin sensitizers.

As indicated previously, Riveley discloses (e.g., col 4, line 50+) a composition comprising insulin and an insulin sensitizer. As stated (col 4, line 56+), the effect of the insulin sensitizer is to sensitize the cells of the mammal so as to enhance insulin uptake and/or utilization of glucose by the cells of the mammal thus reducing the therapeutic dose of insulin that is required.

The response filed 6/15/04 does not traverse this rejection separately from that of the §103 over Walter in view of Rieveley, and so the examiner's arguments with respect thereto are incorporated by reference herein.

The rejection is maintained.

✧

Claims 2, 3 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Walter H. M. (*Diabetes Research* **13** (2) 75-7, 1990) in view of Rieveley (USP 6,153,632), further in view of Thurow H (*Diabetologia* **27** (2) 212-8, 1984).

As indicated previously, Walter discloses (page 76, col 1, paragraph 2) "HOE 21 PH" insulin which is insulin combined with the surface-active stabilizer polyethylene - polypropylene glycol. Also disclosed (e.g., page 76 col 2) is that use of the "HOE 21 PH" insulin resulted in less catheter occlusion and a "significant improvement of metabolic control". Walter does not suggest combining insulin with an insulin sensitizer. Walter also does not state that the surface-active stabilizer is present "in an amount affording a concentration less than the CMC of said composition".

As indicated previously, Rieveley discloses (e.g., col 4, line 50+) a composition comprising insulin and an insulin sensitizer. As stated (col 4, line 56+), the effect of the insulin sensitizer is to sensitize the cells of the mammal so as to enhance insulin uptake and/or utilization of glucose by the cells of the mammal thus reducing the therapeutic dose

of insulin that is required. Rieveley does not teach combining insulin with the surface-active stabilizer polyethylene - polypropylene glycol.

Thurow discloses that combining insulin with Genapol (a block copolymer of propylene oxide/ ethylene oxide) stabilizes insulin. Also disclosed is that the optimal quantity of Genapol is 0.001%, and moreover, that this concentration of 0.001% is below the CMC of genapol (p. 214, col 1, last eight lines). Thurow does not disclose that genapol will have the effect of reduced catheter occlusion or a "significant improvement of metabolic control". Thurow also does not suggest combining insulin with an insulin sensitizer.

Thus, the endocrinologist of ordinary skill would have been motivated to use the surface-active stabilizer polyethylene - polypropylene glycol in order to reduce catheter occlusion and to achieve a "significant improvement of metabolic control" and would have been motivated to use a concentration of the block copolymer which is below the CMC. The endocrinologist of ordinary skill would have been motivated to use the insulin sensitizer to enhance insulin uptake and/or utilization of glucose by the cells of the patient. Thus, by combining the teachings of Walter, Rieveley and Thurow, the artisan of ordinary skill would have arrived at the claimed composition. The claims are thus rendered obvious.

✧

Claims 2, 3 and 21 are rejected under 35 U.S.C. §103 as being unpatentable over Thurow H (*Diabetologia* **27** (2) 212-8, 1984) in view of Rieveley (USP 6,153,632).

Thurow discloses that combining insulin with Genapol (a block copolymer of propylene oxide/ ethylene oxide) stabilizes insulin. Also disclosed that such stability would be advantageous in conjunction with programmable delivery devices. Also disclosed is that the optimal quantity of Genapol is 0.001%, and moreover, that this concentration of 0.001% is below the CMC of genapol (p. 214, col 1, last eight lines). Thurow does not suggest combining insulin with an insulin sensitizer.

As indicated previously, Rieveley discloses (e.g., col 4, line 50+) a composition comprising insulin and an insulin sensitizer. As stated (col 4, line 56+), the effect of the insulin sensitizer is to sensitize the cells of the mammal so as to enhance insulin uptake and/or utilization of glucose by the cells of the mammal thus reducing the therapeutic dose of insulin that is required. Rieveley does not teach combining insulin with the surface-active stabilizer polyethylene - polypropylene glycol.

As indicated above the §103 over Walter in view of Rieveley, the requirement for an "insulin analog" is met, and also the requirement for an "insulin related peptide".

Thus, the endocrinologist of ordinary skill would have been motivated to use the surface-active stabilizer polyethylene - polypropylene glycol in order to reduce adsorption to surfaces when using programmable delivery devices. The endocrinologist of ordinary skill would have been motivated to use the insulin sensitizer to enhance insulin uptake and/or utilization of glucose by the cells of the patient. Thus, by combining the teachings of Thurow and

Rieveley, the artisan of ordinary skill would have arrived at the claimed composition.

The claims are thus rendered obvious.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

✷

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached at 571-272-0925. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

D. Lukton 6/23/04

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600